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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,751	03/26/2004	David S. F. Young	2056.039	9077

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EXAMINER	
REDDIG, PETER J	
ART UNIT	**PAPER NUMBER**
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/810,751	YOUNG ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26 and 29-40* is/are pending in the application.

4a) Of the above claim(s) *6-10,17-21 and 29-40* is/are withdrawn from consideration.

5)☒ Claim(s) *12 and 14* is/are allowed.

6)☒ Claim(s) *1-5,11,13,15,16 and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed June 6, 2007 in response to the Office Action of December 6, 2006 is acknowledged and has been entered. Previously pending claims 27 and 28 have been cancelled, claims 1-5, 11-16, and 22-26 have been amended, and claims 6-10, 17-21, and 29-40 have been previously withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

2. Claims 1-5, 11-16, and 22-26 are currently being examined.

3. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 2, 4, 13, 15, 24, and 26 remain rejected under 35 U.S.C. 112 second paragraph, for the reasons previously set forth in the Office Action of December 6, 2006, page 9.

Applicants argue that claims 2, 4, 13, 15, 24, and 26 are rejected as being indefinite because it recites the phrase a "chimerized antibody". The claims have been modified to state that the antibody is "chimeric". The exact meaning of a chimeric antibody is well known. The process for engineering antibodies, whether humanized or chimeric, is well-described, for example the reference to Winter et al (of record) describes first generation humanized antibodies as simple chimeric mAbs. It is submitted that given the state of the art, such terminology is understood, and such antibodies are obtainable through routine experimentation of a skilled artisan. Thus the metes and bounds of the claim protection sought are readily determined, and it is respectfully requested that this ground of rejection be withdrawn.

Applicants' arguments have been carefully considered, but have not been found persuasive. Although the process for making specific types of chimeric antibodies is well known in the art, the amended claim still encompasses monoclonal antibodies fused to non-immunoglobulin proteins as well as antibodies wherein any domain of the antibody is substituted by corresponding regions or residues of human antibodies including but not limited to CDR grafted antibodies. In the absence of a specific, limiting definition in the specification the metes and bounds of the claims still cannot be determined and Applicant's arguments have not been found persuasive and the rejection is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 23-26 remain rejected and amended claims 1-5 and 11 are rejected under 35 U.S.C. 112 first paragraph, for the reasons previously set forth in the Office Action of December 6, 2006, pages 10-13.

Applicants argue that the specification teaches, based on mass spectroscopic identification combined with the confirmatory immunoprecipitation, western blotting experiments using known CD63 antibodies, and testing the reactivity of PTA-4890 against different isolated extracellular domains of CD63, that the antigen for PTA-4890 is CD-63 and PTA-4890 binds the extracellular region of CD63 encompassing amino acids 108-202, see p. 40, lines 21-23, Example 2, and Fig. 4-9

Applicants' arguments have been carefully considered, but have not been found persuasive. Although the specification has identified that CD-63 is the antigen for PTA-4890

and that PTA-4890 binds to the extracellular domain of CD-63, the single example of CD-63 binding to PTA-4890 does not provide sufficient guidance for one of skill in the art to predictably make an antibody that has in vitro cytotoxic properties against malignant tumor cells and binds to an extracellular region encompassing amino acids 108-202 of CD-63 that can be used for treating a patient suffering from human breast or prostate cancer. Although one of skill in the art could make an a monoclonal antibody to amino acids 108-202 of CD-63, given that it is not clear from the teachings of the specification what the in vitro cytotoxic properties are and given that (as previously set forth) the only exemplified antibody, PTA-4890, is only cytotoxic to 29% of the tumor cells to which it binds, one of skill in the art could not predictably make an antibody that will function as claimed with in vitro cytotoxic properties against malignant tumor cells without undue experimentation. Although Applicant might argue that one of ordinary skill could screen for antibodies that would function as claimed, screening assays do not enable the claimed invention because the court found in (*Rochester v. Searle*, 358 F.3d 916, Fed Cir. 2004) that screening assays are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention. Given that one of skill in the art cannot predictably make the antibody that would function as claimed, upon which the claimed method depends, one could not predictably use the method as claimed without undue experimentation.

Applicants argue that the specification teaches that PTA-4890 was specifically cytotoxic in breast and prostate tumor cell lines selectively, and did not affect normal cells in *in vitro* assays, see p. 42, lines 20-22 and Table I. The specification teaches that PTA- 4890 had cytotoxic activity against the breast cancer cell lines MCF-7 and PC-3 prostate cancer cell line,

but not the MDA-MB-468, MDAMB-231, HT-29, SWII6, SW620, NCI H460 tumor cell lines, see Table I.

Applicants' arguments have been carefully considered, but have not been found persuasive. Although the specification teaches the specific cytotoxic activity of PTA-4890, the exemplification of this single antibody is not sufficient for one of skill in the art to predictably make an antibody with in vitro cytotoxic properties against malignant tumor cells for the reasons set forth above and previously. Given that one of skill in the art cannot predictably make the antibody that would function as claimed, upon which the claimed method depends, one could not predictably use the method as claimed without undue experimentation.

Applicants argue that the specification teaches that PTA-4890 displayed specific tumor binding to the MCF-7, PC-3, MDA-MB-468, MDA-MB-231, HT-29, SWII6, SW620, and NCI H460 and other tumor cell lines, see Table 2. The specification teaches that there was also binding of PTA- 4890 to non-cancer cells, however that binding did not produce cytotoxicity. The specification teaches that this was further evidence that binding was not necessarily predictive of the outcome of antibody ligation of its cognate antigen, and was a non-obvious finding. The specification teaches that this suggested that the context of antibody ligation in different cells was determinative of cytotoxicity rather than just antibody binding, see para. bridging p. 44 and 45.

Applicants' arguments have been carefully considered, but have not been found persuasive. Although the specification teaches the specific cytotoxic activity of PTA-4890, the exemplification of this single antibody is not sufficient for one of skill in the art to predictably make an antibody with in vitro cytotoxic properties against malignant tumor cells for the reasons

set forth above and previously. Given that one of skill in the art cannot predictably make the antibody that would function as claimed, upon which the claimed method depends, one could not predictably use the method as claimed without undue experimentation.

Applicants argue that the claims have thus been amended to be limited to treating a patient suffering from **human breast or prostate cancer** or for mediating cytotoxicity of a **human breast or prostate tumor cell** with a monoclonal antibody or antigen binding fragment thereof which **has *in vitro* cytotoxic properties against malignant tumor cells and** binds to an extracellular region encompassing amino acids 108-202 of CD63 expressed by said breast or prostate cancer, which region is bound by the isolated monoclonal antibody produced by the hybridoma cell line deposited with the ATCC as PTA-4890.

Applicants' arguments have been carefully considered, but have not been found persuasive. Although the specification teaches the specific cytotoxic activity of PTA-4890 towards breast and prostate cancers and that PTA-4890 recognizes amino acids 108-202 of CD-63, the exemplification of this single antibody is not sufficient for one of skill in the art to predictably make an antibody with in vitro cytotoxic properties against malignant tumor cells for use in the claimed method. Although one of skill in the art could make an a monoclonal antibody to amino acids 108-202 of CD-63, given that it is not clear from the teachings of the specification what the in vitro cytotoxic properties are and given that (as previously set forth) the only exemplified antibody, PTA-4890, is only cytotoxic to 29% of the tumor cells to which it binds, one of skill in the art could not predictably make an antibody that will function as claimed, with in vitro cytotoxic properties against malignant tumor cells, without undue experimentation. Although Applicant might argue that one of ordinary skill could screen for antibodies that would

function as claimed, screening assays do not enable the claimed invention because the court found in (*Rochester v. Searle*, 358 F.3d 916, Fed Cir., 2004) that screening assays are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention. Given that one of skill in the art cannot predictably make the antibody that would function as claimed, upon which the claimed method depends, one could not predictably used the method as claimed without undue experimentation.

Applicant's arguments have not been found persuasive and the rejection is maintained.

6. Claims 5 and 16 remain rejected under 35 U.S.C. 112 first paragraph, for the reasons previously set forth in the Office Action of December 6, 2006, section 19, pages 20-21.

Applicants argue that the additional similar grounds of rejection under 35 USC 112 are likewise deemed to be obviated by the instant amendments to the claims.

Applicants' arguments have been carefully considered, but have not been found persuasive, because antigen binding fragments cannot predictably mediate antibody dependent cellular cytotoxicity for the reasons previously set forth.

Applicant's arguments have not been found persuasive and the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-5, 11, and 22-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to methods using monoclonal antibodies, which have *in vitro* cytotoxic properties against malignant tumor cells. It is unclear from the teachings of specification what the *in vitro* cytotoxic properties are. Are the *in vitro* cytotoxic properties cell killing? Or are the *in vitro* cytotoxic properties simply the induction of genes or some other change in cellular phenotype associated with cytotoxicity? Thus the metes and bounds of the claims cannot be determined.

Additionally, the claims are indefinite because the claims require binding to an extracellular region encompassing amino acids of 108-202 of CD-63. It is indeterminate as to what extracellular region is encompassing amino acids 108-202, is the extracellular domain of CD63 or some other protein. Thus the metes and bounds of the claims cannot be determined.

Additionally, Claim 22 recites the limitation "said method of production" in reference to claim 12. There is insufficient antecedent basis for this limitation in the claim.

8. Claims 1-5, 11 and 23-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-5, 11 and 23-26 are broadly drawn to treating a patient suffering from human breast or prostate cancer or for mediating cytotoxicity of a human breast or prostate tumor cell

with a monoclonal antibody or antigen binding fragment thereof which has *in vitro* cytotoxic properties against malignant tumor cells and binds to an extracellular region encompassing amino acids 108-202 of CD63 expressed by said breast or prostate cancer, which region is bound by the isolated monoclonal antibody produced by the hybridoma cell line deposited with the ATCC as PTA-4890. It is noted that does not define what the in vitro cytotoxic properties against malignant tumor cells are.

The state of the art is such that it is well know in the art identifying novel therapeutics for cancer is unpredictable. In particular, Gura (Science, 1997, 278:1041-1042, previously cited) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models that only 29 have actually been shown to be useful for chemotherapy (p. 1041, see 1st and 2nd para.). Furthermore, Kaiser (Science, 2006, 313, 1370) teaches that 90% of tumor drugs fail in patients, see 3rd col., 2nd to last para. Additionally, Young et al. (US Patent Application Pub. 20040180002, September 15, 2004) teach that there have been many clinical trials of monoclonal antibodies for solid tumors. In the 1980s there were at least 4 clinical trials for human breast cancer which produced only 1 responder from at least 47 patients using antibodies against specific antigens or based on tissue selectivity. Young et al. teach that It was not until 1998 that there was a successful clinical trial using a humanized anti-her 2 antibody in combination with cisplatin (para 0010 of the published application). The same was true in clinical trials investigating colorectal cancer with antibodies against glycoprotein and glycolipid targets, wherein the specification specifically teaches "to date there has not been an antibody that has

been effective for colorectal cancer. Likewise there have been equally poor results for lung, brain, ovarian, pancreatic, prostate and stomach cancers" (para 0011 of the published application).

Given the above and in the absence of a definition of what the *in vitro* cytotoxic properties are, it is evident that the specification does not provide a written description of the broadly claimed antibody that is useful for a method for the treatment of breast or prostate cancer or for mediating cytotoxicity of breast or prostate cancer cells for the reasons set forth below.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics.... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of an antibody with *in vitro* cytotoxic properties against malignant cells that binds to an extracellular region encompassing amino acids 108-202 of CD63 that is useful for treating a patient suffering from a human breast or prostate cancer or mediating cytotoxicity of a human breast or prostate tumor cell per Lilly by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus". Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe antibodies with *in vitro* cytotoxic properties against malignant cells that bind to an extracellular region encompassing amino acids 108-202 of CD63 that is useful for treating a patient suffering from a human breast or prostate cancer or mediating cytotoxicity of a human breast or prostate tumor cell in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of the antibody with *in vitro* cytotoxic properties against malignant cells that binds to an extracellular region encompassing amino acids 108-202 of CD63 that is useful for treating a patient suffering from a human breast or prostate cancer or mediating cytotoxicity of a human breast or prostate tumor, nor does the specification provide any partial structure of an antibody with *in vitro* cytotoxic properties against malignant cells that binds to an extracellular region encompassing amino acids 108-202 of CD63 that is useful for treating a patient suffering from a human breast or prostate cancer or mediating cytotoxicity of a human breast or prostate tumor,

nor any physical or chemical characteristics of the said identifying characteristics nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses that one of the PTA-4890 antigens is CD63, the binding of CD63 by PTA-4890 does not appear to be sufficient for the cytotoxic function of PTA-4890. Thus this does not provide a description of the antibody with *in vitro* cytotoxic properties against malignant cells that binds to an extracellular region encompassing amino acids 108-202 of CD63 that is useful for treating a patient suffering from a human breast or prostate cancer or mediating cytotoxicity of a human breast or prostate tumor.

The specification also fails to describe the antibody with *in vitro* cytotoxic properties against malignant cells that binds to an extracellular region encompassing amino acids 108-202 of CD63 that is useful for treating a patient suffering from a human breast or prostate cancer or mediating cytotoxicity of a human breast or prostate tumor by the test set out in Lilly. Although the specification discloses that the PTA-4890 antigen is CD63, the binding of CD63 by PTA-4890 does not appear to be sufficient for the cytotoxic function of PTA-4890. Therefore, it necessarily fails to describe a "representative number" of antibodies with *in vitro* cytotoxic properties against malignant cells that bind to an extracellular region encompassing amino acids 108-202 of CD63 that are useful for treating a patient suffering from a human breast or prostate cancer or mediating cytotoxicity of a human breast or prostate tumor. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the antibodies with *in vitro* cytotoxic properties against malignant cells that bind to an extracellular region

encompassing amino acids 108-202 of CD63 that are useful for treating a patient suffering from a human breast or prostate cancer or mediating cytotoxicity of a human breast or prostate tumor that is required to practice the claimed invention or reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the broadly claimed invention. Since the specification fails to adequately describe or reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the broadly claimed invention that is the broadly claimed antibodies with *in vitro* cytotoxic properties against malignant cells that bind to an extracellular region encompassing amino acids 108-202 of CD63 that are useful for treating a patient suffering from a human breast or prostate cancer or mediating cytotoxicity of a human breast or prostate tumor, it also fails to adequately describe the claimed method or reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Further, the following teaching of the court as set out in Noelle also clearly applies to the instant claimed invention. The court teaches as follows: "Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle

only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application. Moreover, Noelle cannot claim the genus form of CD40CR antibody by simply describing mouse CD40CR antigen". *Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin* (CAFC, 02-1187, 1/20/2004). The findings of Noelle apply to the claimed antibody of the methods of claims 1-5, 11 and 23-26 as Applicants are claiming unknown antibodies against an unknown antigen, an antibody that binds to an extracellular region encompassing amino acids 108-202 of CD63. Since an antibody is defined by its antigen binding capability and Applicants have only exemplified PTA-4890 that binds to amino acids 108-202 of CD63, Applicants have not provided an adequate written description of the antibodies that binds to an extracellular region encompassing amino acids 108-202 of CD63.

9. All other objections and rejections recited in the Office action of November 21, 2006 are withdrawn.

10. Claims 1-5, 11, 13, 15, 16 and 22-26 remain rejected.

11. Claims 12 and 14 appear allowable in their current form.

12. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to

the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal form, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

13. Applicants' amendments necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE

ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. ' 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

Peter J. Reddig
Examiner
Art Unit 1642

PJR